THE SIGNIFICANCE OF STIMULATION IN THE DEVELOPMENT OF THE NERVOUS SYSTEM

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The unit in the nervous system is the neurone. It is now pretty generally accepted that this unit—made up of the cell body and its processes, the protoplasmic processes, or dendrites, that convey nervous impulses to the cell body, and the nerve fiber, axon or neurite, that conducts nervous impulses from the cell body,—is an anatomical unit, a functional unit, a trophic unit, and a genetic unit. The nervous tissue is made up of millions of such neurones. But all are functionally connected and integrated into a system. The child has as many neurones as the adult, but they are undeveloped.

It has long been known that stimulation is a condition of development in the nerve centers. The classic investigations by Held and others have shown, too, that stimulation hastens development. More recent studies have shown not only that the development of the nervous system in the individual and in the philogenetic series has been conditioned by stimulation from the external world, but also that function and stimulation have been fundamentally significant in the development of the individual neurones. It is the purpose of the present paper to trace briefly some phases in the development of the nervous system as determined by stimulation.

Our knowledge of the genesis of nervous tissue is still inadequate. It seems, however, most in harmony with the knowledge we have, to suppose that it developed *pari passu* with the growing complexity of reactions to the stimuli of the environment. Thus with the reactions similar to the tropisms and the like in primitive animals there developed a mechanism for coördinating such reactions. In general this development has taken place in connection with the function of reacting to stimulation. In certain lower orders of animals, the corals, for example, nerve cells and fibres are evenly distributed to the whole surface of the body. In other animals, those parts most favorably located for receiving impressions from external objects become more richly supplied with nerve cells (29).

In the medusa this location is the rim of the bell. In the echinoderms it is around the mouth, and here is developed a

ring of nerves. The bell rim of the medusa, and the oral ring of the echinoderms with its radiating paths, represent a central nervous system with which the rest of the nerves may be contrasted as peripheral. Thus the nervous substance originates in contact with the stimuli of the external world.

Again, in the embryo the nervous substance is formed, not from the mesoblast, but from the outer germ layer, the ectoderm or epiblast, in response, as it were, to external stimuli, and then folded in to form the nerve tube, the original form of the central nervous system.

Thus both in the individual and in the phylogenetic series the nervous system seems to have been developed under the stimulus of the external world. As the nervous system becomes more and more complex we find certain special structures or special organs developed in connection with the reaction to certain stimuli; and finally, we have the marvelous mechanism of the human brain and its connections with the external world.

From the functional point of view Herrick (12, p. 36) has summarized the evolution of the nervous mechanism as follows:

"The functions which characterize the nervous system have been derived from those of ordinary protoplasm by further development of three of the fundamental protoplasmic properties, viz., sensitivity, conductivity, and correlation. The most primitive form of nervous system known is diffuse and local in its action, but in all the more highly developed forms the chief nervous organs tend to be centralized for ease of general correlation and control. Most of the types of nervous systems found in the animal kingdom are represented in two distinct and divergent lines of evolution, one adapted especially well for the reflex and instinctive mode of life and found in the worms, insects, and their allies, and the other found in the vertebrates and culminating in the human brain with its remarkable capacity for individually acquired and conscious functions."

The great function of the nervous system from the physiological point of view is the coördination and integration of movement and the adaptation of reaction to sensory-motor experience. This has been shown in detail by Sherrington and others (23a).

As has often been pointed out, the nervous system is a mechanism for converting stimuli into reactions. It has been customary to look upon the reflex arc as the type of all that is accomplished by the nervous mechanism. The essential parts of the process are three: first, an incoming nervous current along an afferent or sensory nerve; second, a central process more or less complicated; third, an outgoing nervous current along an efferent or motor nerve to innervate a muscle

or a gland. All the accomplishments of the nervous system have usually been described as reflexes or combinations of reflexes.

To take a concrete case, the classic illustration is as follows: If one puts a drop of acid on the thigh of a decapitated frog, immediately the leg is drawn up in the attempt to brush off the irritating substance. Here we have an example of the simple reflex arc. The course of the nervous impulse is briefly as follows: The nervous impulse caused by the stimulation of the nerves of touch in the frog's thigh is carried by the afferent sensory nerves to the sensory cells in the dorsal part of the cord, then the impulse is transferred by the central nervous processes to the motor ganglion cells in the ventral part of the cord, and the excitation of them causes an outgoing nervous current along the efferent or motor nerve which innervates the muscles of the frog's leg.

The essential elements of the anatomical structure involved in a reflex are three: first, a receptor or sensory receiving organ; second, a connector, or adjustor, the nervous tissue connecting the afferent nerve with the efferent or motor nerve; and third, the effector, consisting of the mechanism of response. Or we may divide the mechanism more concretely as Herrick (12, p. 25) does, into five parts as follows:

"(1) A sensitive receiving organ (receptor or sense organ); (2) a conductor (afferent or sensory nerve) transmitting the nervous impulse inward from the receptor; (3) a correlation center or adjustor, generally located within the central nervous system; (4) a second conductor (efferent or motor nerve) transmitting the nervous impulse outward from the center to (5) the effector apparatus, consisting of the organs of response (muscles, glands) and the terminals of the efferent nerves upon them."

The sequence in the development of this mechanism is not altogether clear. The studies of sponges and other lower forms of animal life by Parker and others, however, indicate that the muscle preceded the nerve in its evolution and was the first element of the reflex arc to be developed. Sponges, for example, represent animals with effectors without differentiated receptors. Evidence is furnished also by certain reactions in the higher animals. To quote Parker (22, p. 124):

"If muscle originated before nerve and was brought into action at first by direct stimulation, it is natural to expect that examples of this form of response might still be found among the higher animals. And such seems to be the case. Thus the sphincter of the iris in the lower vertebrates, though well known to be under the influence of nerves, was shown by Steinach some time ago to be directly stimulated by light, a condition which, judging from the more recent work of Hertel, probably applies even to the human eye. This muscle then exhibits a certain

capacity for normal direct stimulation. Another example of the same kind is seen in the embryonic vertebrate heart. Though the beat of the adult heart may be a matter of controversy from the standpoint of the myogenic and neurogenic theories, there can be no doubt that the muscle of the embryonic heart beats, as shown by His, before it has become invaded by nerves. And this view is supported by Barrow's recent discovery that the isolated cells of the heart-muscle will contract rhythmically under conditions where not the least vestige of a nerve can influence them. Thus the embryonic heart-muscle and the sphincter of the iris are muscles whose activity may be normally called forth by direct stimulation, a condition which reproduces, so far as independence is concerned, the state met with in the muscles of the sponges. These examples then show that even in the higher animals certain muscles respond normally to direct stimulation and thus exhibit a form of activity which is believed to be generally characteristic of sponges."

A good example of a very primitive form of nervous system is that found in the sea-anemones. As described by Parker (22, p. 121), these are sac-like animals with a single opening leading into the digestive cavity. The animal has no well-defined organs except the digestive apparatus and is merely a membranous digestive sac. The body of the sea-anemone, however, contains both nerve and muscle, occurring over almost the whole of the animal. Each part seems to carry its own neuro-muscular mechanism. The nervous system in the sea-anemone is diffused rather than centralized. No part of the animal's nervous organisms seems to be more important than any other part; it consists of a vast number of sensory neurones which connect the surface of the animal with the underlying muscles. Its function is merely the reception of stimuli and the immediate excitation of the muscles. The nervous mechanism is a receptor that acts as a trigger for setting off the muscle. That is, the animal consists merely of receptors and effectors without the intervention of an adjustor or a central organ.

Afterward as these receptors became more highly developed, the third element, the central nervous element, was evolved. This serves as an adjustor, a means of connection and correlation between the receptor and the effector. Thus the order of development was: first, the effector; second, the receptor; and third, the adjustor or central organ.

Thus the nervous system originated "at spots," probably where the animal had developed muscle, and was later unified. As Parker has expressed it (22, p. 127):

"Although the nervous system probably arose in a scattered way at spots where the primitive multicellular animal had developed muscle, it became unified through the need for general transmission tracts, and, by increasing its own elements as well as by appropriating additional

effectors and receptors, it has impressed upon the higher animals, including ourselves, a unity so profound that it includes everything that we mean by personality."

Another class of recent investigations show that there are kinds of nervous action not adequately described as reflexes at all. Hough, in a recent paper, distinguishes the following classes of nervous action: automatic, axon reflex, unconditioned reflex, conditioned reflex, and volitional. For the present purpose it will be sufficient to note the automatic, unconditioned reflex, and conditioned reflex action of the nervous substance, and here we may well follow Professors Hough and Brown (14, p. 410):

"In the central nervous system the best known and most successfully studied case of automatism is that of the respiratory center. The conclusion which Rosenthal drew from his experiments, that the nerve cells of this center send out rhythmic discharges when removed from all connection with afferent nerves, has been confirmed by all subsequent work, the experiments of Winterstein being especially conclusive on this point."

"The work of T. Graham Brown suggests that the same thing is true of the rhythmic movements of locomotion. Brown shows that in a certain stage of ether narcosis in the decerebrate animal, when reflexes can no longer be elicited from the afferent nerves, rhythmic movements of flexion and extension occur in the hind legs; and furthermore, that these movements occur after the afferent nerves from the moving limbs are cut. In other words, these movements which suggest the basis of the movements of locomotion, involving as they do the alternate rhythmic action of antagonistic groups of muscles, are executed by efferent neurones without any stimulation from afferent neurones. They constitute 'an endless chain,' but not an endless chain of reflexes."

Brown (14, p. 411) raises the question whether these automatic actions of locomotion do not present a more primitive form of nervous activity than the reflex. He suggests that "the nervous mechanism of locomotion, like the nervous mechanism of respiration, is fundamentally an automatic mechanism. Later on afferent neurones are added to it, comparable to those of the pulmonary branches of the vagus. In this connection it is most significant that in general the same conditions so frequently referred to as stimuli of the respiratory center—lack of oxygen, excess of carbon dioxide, etc.—are the very conditions found to favor the movements of narcosis progression."

Apparently in such automatic nervous action we have nervous action without stimulation. The exception is, however, strictly more apparent than real. It would, perhaps, be better to say that in case of automatic nervous action the stimulus is within the central nervous organ itself instead of being carried to it by a receptor organ. Especially if we take

Verworn's definition of a stimulus (27), as any change, we are justified in taking this view. The automatic nervous action is like all other nervous action, response to stimulation, but in this case the stimulus is internal.

As the highest form of nerve action we have the association of stimuli in the production of conditioned reflexes. As shown by the Russian school of Pavlov, in the higher animals the stimulus from any receptor organ may become associated with the natural or biologically adequate stimulus that produces a given reaction and produce the same reaction. This is called a conditioned reflex in contrast with the ordinary or unconditioned reflex. The difference between the one and the other may be very simply illustrated.

If you give your dog a piece of meat a secretion of saliva occurs. This is an ordinary reflex. If every time you feed your dog meat you ring a bell, after a little while you can ring the bell without giving the meat and there will be a flow of saliva. The ringing of the bell has become associated with the stimulus of the meat and produces the same reaction. Such an associated stimulus is called a conditioned stimulus, and the reaction produced, a conditioned reflex. This is a most remarkable phenomenon. An entirely indifferent stimulus associated with the ordinary stimulus produces the same physical effect. This association is effected by the brain cortex.

Thus, as the genetic sequence for the elements of the reflex arc is: first, the effector; second, the receptor; and third, the adjustor; so in its simplest form the genetic sequence of the different forms of nervous action is probably as follows: automatic action, reflex action, conditioned reflex action.

A helpful distinction for the genetic point of view is that between the paleencephalon, or old brain, and the neëncephalon, or new brain, sometimes called the pallium or brain mantle. As Edinger (5, p. 12) expresses it: "The most important thing of general significance which comparative anatomy teaches is this, namely, that the whole mechanism of the spinal cord up to the olfactive nerve is in case of all the higher and lower vertebrates similarly organized; that therefore for the simplest functions through the whole series a similar basis exists whether it is a question of man or fish. This fundamental part of the brain, the old part, we may call the paleencephalon." In contrast with this is the more recently developed part of the brain, the neëncephalon, or the brain cortex and its dependencies.

Neëncephalon in black
Paleëncephalon in gray
(After Edinger)

The former, the paleëncephalon, was the original brain. It consists of the cerebellum and the brain stem; and the neëncephalon consists of the part of the brain superimposed on these basal portions, the cortex and its dependencies. Hence the name brain mantle.

The paleëncephalon mediates movements, the reflexes, and many instincts. Locomotion, posture, the processes of nutrition and other vital processes are controlled by it. The neëncephalon, on the other hand, mediates the functions of association and the higher mental processes.

Not only the old brain but also the new brain has developed in behoof of adjustment to the environment. In Edinger's words (6):

"Wherever we investigate, everywhere the development of separate parts of the paleëncephalon appear dependent altogether on the manner of life. Traces of the neëncephalon, an apparatus which folds itself over the paleëncephalon, appear in the case of selachians, and become greater in case of the amphibians. In a continuous series it increases through the amphibians up to the mammals, and in the latter it develops to the enormous structure which in case of man becomes the bearer of all the higher mental functions. If we divide all actions into those of the paleëncephalon and those of the neëncephalon according as they are performed by one or the other of the two great divisions of the brain, we acquire a principle of classification and study for comparative psychology."

While no hard and fast divisions occur in neurological development, any more than dramatic epochs are found in psychological evolution, we do find with the appearance of the neëncephalon a new form of behavior, and new possibilities for the development of intelligence. Fishes have only the paleëncephalon. The rudiments of the neëncephalon are found in selachians and amphibians. The neëncephalon appears definitely in reptiles. And as Edinger (6, pp. 453-4) says:

"Finally, in the mammals we meet a brain which has so large a neëncephalon that we may well expect a subordination of reflexes and instincts to associative and intelligent actions. That, in fact, is the case with those mammals in which the neëncephalon includes much more than half the bulk of the entire brain. But in many families there is very little advance beyond the condition prevailing in birds, for example, in the hedgehogs and the moles. In the mice, the rabbits, in fact in nearly all the rodents, the two parts are about evenly balanced. What we know of the intelligence of these animals—and that is little enough—is in very close accord with the condition of the brain."

Again, as Edinger (6, p. 447) has pointed out, a distinct advance appears with the advent of the neëncephalon. This change of behavior is especially noteworthy in the activities related to the taking of food.

"Hungry animals," he notes, "if they possess only the paleëncephalon seize food under all circumstances, provided the stimuli which proceed from it are appropriate, but only then. An animal which is incited to seizing only by a moving body never recognizes the same body if it is at rest. All of these animals can be caught with bait if one has ascertained the proper stimulus. Fishes which, like the trout, go toward

swiftly moving and glittering insects can be caught by imitations of such insects constructed of metal and feathers, providing the angler rightly imitates the hopping movement. The entire art of angling, concerning which we possess large volumes, depends upon knowledge of the proper stimulus and upon the excluding of disturbing stimuli, such for example as a thick fish-line. Frogs may be caught by means of heath-berries dangled before them on a string. Even the frog has a rudimentary neëncephalon, but so far as my observations go, it plays no part in the obtaining of food. It still eats paleëncephalically. No matter how hungry a frog may be, it seizes the earthworm only when it crawls, or catches the fly only when it makes some movement. One may lay a worm on the frog's snout or may in any way bring the two in contact, but eating does not result. The worm acts as a stimulus only when crawling, otherwise it is not recognized."

Thus while the paleëncephalic animal is stimulated by its prey only when the latter moves, serpents, on the other hand, once stimulated by a jumping frog or a running mouse follow their prey, at least for a time, and are able, perhaps by the olfactory sense, to find a particular hole into which the prey has crept. Lizards and serpents also assume an attitude of defense when danger threatens. They direct the head toward the enemy and attempt to bite. Edinger says he has never observed anything of this kind in a paleencephalic animal. Among reptiles also for the first time one meets with individual differences; in the same species there are indolent and excitable individuals; this, too, is probably due to the neëncephalon. And finally, reptiles learn more easily than fishes. Again to quote Edinger (6, p. 450):

"Most important in the psychological behavior of reptiles is the fact that the animals are no longer always dependent upon the sense impression of the moment, but that earlier impressions influence them. Further, they associate certain sense impressions which lie within the realm of the olfactory and oral senses, and turn them to account; they learn more easily than fishes and amphibians; occasionally they foresee; and they exhibit individual differences. There can be no doubt that all of these facts are referable to the appearance of a cortex in the neëncephalon."

Edinger sums up his view of the relations between the structure of the nervous system and its activity in substance as follows (5, p. 221): The paleëncephalon functions impressions and motions, often of a very complicated sort. Above these is developed in continually increasing degree with the growth of the cortex the ability for knowing and doing. This has its basis in the sense centers of the cortex, an apparatus to which we must ascribe the ability of coördinating the impressions that come from the paleencephalon with numerous others in such a way that it can inhibit and again reproduce them if similar or related impressions stimulate it. Thus knowing leads to doing.

Separate parts of the cortex are more directly connected with the peripheral sensory apparatus, others more with the peripheral motor apparatus. With these parts of the brain are associated other areas of the cortex, especially in the frontal lobe; and with the appearance of this, the intelligence first appears clearly, along with knowing and doing.

The reactions brought about by the paleëncephalon in response to stimuli, the actions which proceed from the sense centers on occasion of perceptions, are similar in case of man and animals. Indeed, the animal is sometimes far superior to man in both of these. Only one thing is developed in case of man far more than in case of animals, namely, the association centers, especially the frontal lobe; and with this, high intelligence, which presupposes consciousness; but since the frontal lobe is present in different degree even in animals, we are forced to the assumption that many actions of animals must be accompanied by the functioning of this part of the brain. "Comparative anatomy," says Edinger, "becomes here the pathfinder of psychology."

An important point not always noted is the increased scope and importance of cortical control in the higher animals, especially in human beings. The child reported by Edinger (7), born without a neëncephalon, was incapable of the simple functions that a dog deprived of its brain can perform. And apparently many movements that are completely and perfectly executed by the paleëncephalic animal are brought under control of the cortex in the higher animals and man. Thus with greater and greater development in the animal series there is more and more centralization in the neëncephalon. The physical basis for this is apparently the new groups of neurones leading to the cerebrum that are added with greater development. Pike (23, pp. 392, 395) illustrates this as follows:

"It has been shown anatomically and experimentally to some degree, that new groups of nerve cells and fiber tracts appear in the central nervous system as we pass from the lower to the higher vertebrate forms. These new tracts and cell groups lead more and more to the cerebrum or become located in it; hence, the greatest development of the cerebrum and its afferent, efferent and association paths occurs in the human nervous system. As a rather familiar example, the pyramidal tract, arising from cells in the cerebral cortex of the higher vertebrates, may be cited as one of the phylogenetically newer tracts. The frog has no pyramidal tract, but depends upon the rubro-spinal tract as the important part of his motor mechanism.

"In any motor response a great number of afferent impulses of various kinds are involved. It is apparent also that some of these impulses go to the cerebrum almost directly. There is much evidence to show

also that in the higher animals, nearly all other impulses, including those to the cerebellum, get to the cerebrum before they become effective in influencing the motor response."

"Attention shifts therefore, from the afferent pathway to the central system. Somewhere these afferent impulses must be gathered up . . . and passed on to the motor cells directly. The very complexity of the process is sufficient evidence that no one restricted group of cells constituting a hypothetical center could accomplish all of the things to be done. At the present time there is good, and even sufficient, reason for believing that nearly all of these impulses, including those from the cerebellum, pass through the frontal lobes of the cerebrum on their way to the motor neurones. On this view the cerebrum is an essential part of the great motor mechanism. It is in the cerebrum that the summing up or integrating of all the afferent impulses occurs."

Recalling again the reacting function of the nervous system we may note that, among recent writers, Dr. Dearborn (3) maintains that the conception of the reflex arc and of the combination of reflexes give but an inadequate idea of the great complexity of the processes involved, and he thinks that the facts, as we now know them, are better represented by the figure of a circuit and a hierarchy of circuits in which the lower are more or less under the control of the higher. But the facts are even more complex than this.

It is of fundamental importance for the understanding of the genetic point of view, both in neurology and in psychology, to keep in mind the fundamental metabolic and functional processes of the neurones. Not only are the nerve centers and the nervous system as a whole functionally active, their health as well as their efficiency depending upon their functional activity, but even the development of the individual neurone is determined by its metabolism and its functional ability in responding to stimulation. It is well to note briefly here some of the main points in the rather technical contributions made in recent years by the Dutch neurologist Kappers, the Spanish neurologist Cajal, and others.

In 1907 Kappers (1, p. 557) proposed the theory of neurobiotaxis, and in the following year formulated the following laws: 1. If discharge of stimuli occurs in different parts of the nervous substance, then the development of the chief dendrites, and especially the location of the whole body of the ganglion cell, occurs in the direction of the maximal discharge of stimuli.

2. This approximation of dendrites or of cells takes place only between places stimulated simultaneously or in direct succession.

3. The development of the axis cylinder of the so-called central motor system is not conditioned primarily by the motor

function of certain cells, but likewise by the areas stimulated synchronously or successively.

To summarize the law: dendrites and neurites grow in the direction of areas that are stimulated simultaneously with them. This law is in harmony, Kappers maintains, with the psychological law of the association of simultaneous stimuli. Thus he maintains that the fundamental law of psychology is a fundamental law of brain anatomy (1, p. 557).

Kappers has given many illustrations of this law from his studies of phylogeny, illustrations not only for the dendrites, but also for the neurites, and illustrations also of the adjustments or displacement of the cells in connection with this development. Bok (1) in his recent studies has furnished illustrations from the development of the individual. Thus we have now evidence both from phylogeny and ontogeny, which show at least that the processes of the neurones develop especially in the directions of the greatest discharge of stimuli.

Bok has studied the development of the processes in the neurones of chicken embryos, and finds that stimulation is the determining cause of the development of the fibrillae and of the nerve paths. As the result of his studies he has made important corrections to Kappers' law and formulated three general rules in regard to the development of new paths (1, p. 537-539).

1. New paths develop from neuroblasts located near paths that already exist.

2. The young neurone in the beginning has no contact with the path that stimulates it. This is a result of the known fact that the neurite develops sooner than the dendrite. The contact mentioned does not arise until later, by two processes —by the outgrowth of dendrites of the neuroblast and by the formation of collaterals through the path. The activation therefore is in a certain sense a distance-effect, although the distance that is here bridged is a rather small one.

3. The new fibrillae develop in the direction of this stream of stimulation radiating from the path that already exists.

"This coincidence," Bok (1, p. 542) argues, "of the direction of the young fibres, which can be established everywhere, and that of the stimuli coming to them cannot rest on chance, but forces us to consider this stream of stimulation as the cause of the development of the nerve fibres in its direction. The protoplasm located there adapts itself to its function, namely, the conduction of stimuli, by the development of nerve fibrillae. Accordingly this formation of nerve fibrillae and of paths can be referred back to a generally recognized fundamental principle in biology, the adaptation of the protoplasm to repeated function."

Bok formulates his hypothesis of the development of the fibrillae in accordance with this law, as follows (1, p. 542): "Constantly repeated stimuli cause fibrillae to develop along their course."

Every neurite, however, grows with the stream of stimulation, hence away from the cell body, but the dendrite grows in the opposite direction, that is, toward the stream of stimulation. The dendrite is rich in protoplasm, the neurite almost totally free from protoplasm; and we come to the conclusion that protoplasm has the tendency to displace itself in the direction of the stimuli, that is, to seek out the source of stimulation.

Kappers (1, p. 557) showed similarly that the growth of dendrites is determined in the direction of the maximal discharge of stimuli. Thus the ganglion cells in a certain degree are to be compared to the amoeba. The latter sends out its pseudopobia toward the place where the most nourishment is to be found; the nerve cells allow their dendrites to grow in the direction of their functional nutrition, that is, in the direction of their stimulation, and here we can speak of a stimulotaxis just as we do of the chemotaxis in the case of an amoeba.

This displacement of the protoplasm in the direction from which the stimuli come is not always limited to a part of the cell, but can also occur in the whole cell body so that this migrates in the direction of the stream of stimulation in a manner analogous to the movement of the amoeba in the direction of its nutrition. The displacement of the cell therefore occurs in the direction from which the stimuli come, and it is easy to see that thus it occurs in the direction of areas that are simultaneously stimulated, that is, in the direction of the source of the stimuli which stimulate the cells.

Kappers points out that cell-migration in a certain direction is generally preceded by an outgrowth of a large dendrite in which the shifting of the cell takes place. The theory that the dendritic outgrowth follows a preformed plasmodermic path cannot, he maintains, explain the shifting of the cell. His studies, on the other hand, "now covering all the cranial motor nuclei in all classes of vertebrates, have taught him with certainty that for this phenomenon only the process of taxis or tropism exercised by the centres from which the majority of stimuli proceeds to the cell and its dendrites can be considered as responsible." The dendrites therefore demonstrate the law of neurobiotaxis in the manner of their growth.

Kappers (17) in more recent studies has found that the den-

drites are apt to take a shape which gives a maximal amount of surface as a means for enlarging the area for the receptor elements, and he concludes that this surface extension of dendrites of certain cells indicates that here, too, we have to do with a process of neurobiotaxis, a striving for the maximal reception of stimulation in the shortest manner.

Bok (1, p. 561) summarizes his results in substance as follows: If we think of the partially developed nervous system as functioning, the stimuli accumulated in certain paths will radiate from the naked axis fibres into the surrounding protoplasm.

New paths always develop where a diffusion of stimulation of this kind takes place. The young fibrillae develop therefore in the direction of the stimuli, in protoplasm lines which have been marked out by repeated stimulation. They develop hence, from the neuroblast which has been traversed first and is therefore most strongly marked out by paths. This is the basis on which the hypothesis of the generation of fibrillae by stimulation rests.

Repeated streams of stimulation cause fibrillae to develop in their direction. The formation of fibrillae, according to this hypothesis, is in harmony with the general property of protoplasm to adapt itself to a repeated function.

This assumption is supported by the observation that a path at the moment another path appears activates new neuroblast substance along its whole length, from which the neurites again develop in the direction of the stimuli.

Since protoplasm has the tendency to approximate its source of stimulation (positive stimulotaxis), we see that the dendrites are rich in protoplasm, the neurites poor in protoplasm, and that the whole cell body tends to take a position in the direction of the stream of stimuli conducted toward it, that is, according to the law of neurobiotaxis.

This consideration of the history of the development of the system of paths teaches us that the paths do not in the first instance prescribe the way for stimuli, but that it is precisely the stimuli which bring about the configuration of the paths. With the constant action and reaction between structure and function in the central nervous system, function is the primary cause of the arrangement of the anatomical substrate; and thus Bok (1, p. 562) quotes the words of Schiller and says that this gives a deeper meaning to the words of the great German poet: *"Es ist der Geist der sich den Körper bildet"*; "It is the mind which forms the body."

While admitting our ignorance in regard to the poetic interpretation in the closing sentence of Bok's summary, and without attempting to solve that problem of the priority of structure or function, we should note the emphasis upon the influence of function on development brought out by his results.

One is likely at first to fail to recognize the significance of these contributions. If these laws formulated by Kappers and Bok be true, then we have a contribution here of fundamental importance for genetic psychology. Long ago Zanotti and Hume pointed out the fundamental character of the law of association in psychology, comparing it to the law of gravitation in the physical world. Here in the doctrine of the genesis of neural processes and paths we have at least the adumbration of a law equally fundamental for neurology and genetic psychology.

The results of these investigations indicate the neural basis of what Hering (11) long ago called "memory as a universal function of organized matter." This appears as a general property of protoplasm itself, the ability to adapt itself to the functions it performs.

In some such way as the amoeba reacts towards its food, sending out pseudopodia in the direction from which the most nutriment comes, so the protoplasm of the neurone reacts toward the stimuli which affect it, the dendrites growing especially in the direction of the source of stimulation. It is noteworthy that they are the protoplasmic processes of the neurone, and that on the other hand, the neurite or axon, which grows with or in the direction of the stream of stimuli conducted from the cell body, is relatively free from protoplasm.

Just as the reaction of the protoplasm of the amoeba toward its food is called chemotaxis, so the reaction of the protoplasm of the neurone toward the source of stimulation may be called, as suggested by Bok, positive stimulotaxis.

If we add the further evidence of the modification of the neurone by stimulation, from the fact that the cell body itself is sometimes displaced in the direction of the stream of stimulation; that the dendrites show a tendency to spread out in an extended surface in order to give a maximum area for the reception of stimuli; and the fact that the cell body grows with its functional activity, and suffers arrest or atrophies when stimulation ceases; and if we bring into connection with these facts in regard to the development of the neurone the well-known facts in regard to facilitation (2), or what the

Germans call Bahnung, a second application of a given stimulus at a suitable interval having a greater effect than the first, we have an indication of the neural basis of memory and association.

CONCLUSION

The studies by Parker and Brown suggest the probable genesis of nervous action. Further investigations will probably harmonize these results and give more definite knowledge in regard to the early stages and sequence of development of nervous structure and function. As regards the main point the evidence all points in one direction. If we study the philogenetic series, we find that even before the nervous system appears, reaction to the environment is the significant fact, and that probably the nervous system develops at spots where the prim'tive animal developed muscle. If we study the individual we find that in the embryo the nervous substance is developed from the outside layer, the epiblast, where the organism comes in contact with the external world. And if we study the individual neurone we find that its development is determined largely by its functional ability to respond to stimulation, its dendrites especially developing in the direction from which the most stimuli are received.

The significant thing is that all of these studies show what has been emphasized over and over again, namely, the significance of function and the fundamentally dynamic character of every neurone. We find here what we find everywhere as we study the physiology and hygiene of the human organism, that function, action, expenditure of energy, as well as the storing up of energy, are the fundamental conditions of life and health. Function is the Alpha and Omega of individual life as well as of the universe in general, a profound illustration of the words of Goethe, "*In der Anfang war der Tat.*"

While the nervous system is, as the older writers already knew, a mechanism for converting stimuli into reactions, our genetic point of view has shown further the two great divisions of stimuli: On the one hand, those that are biologically adequate; on the other, those that act only by association. The former bring about ordinary reflexes and instinctive activities; the latter bring about conditioned reflexes, habits, and the like. The former are mediated by the paleencephalon, the latter by the neëncephalon.

The ability of neurones stimulated simultaneously to affect each other and the ability of the brain cortex to associate

stimuli carried to it simultaneously by different receptor organs, form the neurological basis for mental association, at once the fundamental law of psychology and the foundation for the whole of mental hygiene.

Thus without going into details we can trace the genetic course of development of the nervous system as a reacting mechanism.

1. The nervous system originated in contact with the external world.

2. It originated in spots where the primitive animal had developed muscle.

3. The sequence of the genesis of the reflex arc was: first, the effector organ; second, the receptor organ; third, an adjusting mechanism connecting and correlating the other elements of the reflex arc.

4. There are different forms of nervous action, especially automatic nervous action, reflex action, and conditioned reflex action.

5. The sequence of development seems to have been: first, automatic nervous action; second, reflex action; third, conditioned reflex action.

6. The central nervous system may be conveniently divided into the paleëncephalon and the neëncephalon. The paleëncephalon mediating reflexes and instinctive actions, and the neëncephalon mediating especially association and knowledge.

7. With the higher stages of development there is more and more of centralization in the neëncephalon and more and more of cortical control.

8. The individual neurones develop their processes in the direction of the greatest discharge of stimuli, the dendrites toward the stream of stimuli, the neurites with the stream of stimuli.

9. We find the neurological basis of association in the working out of paths in the nervous substance between areas simultaneously stimulated.

10. Two kinds of stimuli may be advantageously distinguished: first, those that are biologically adequate, or what may be called unconditioned stimuli; second, those that are associated or may be called conditioned stimuli.

Thus we see from the genesis of the nervous system that the one condition necessary for normal development is a rich environment giving plenty of stimulation and freedom for the nervous mechanism to develop in its own way. This seems especially important for the higher parts of the nervous system, the new brain, or the cerebral cortex and its depend-

ent structures. The same thing is emphasized, too, by all those cases of defect where normal stimuli are shut off. In such cases there is always imperfect or arrested development.

The wider relations and wider significance of stimulation and response are suggested by our survey of the development of the nervous system. When we see the rôle of stimulation in the genesis of the nervous system, it need not seem strange that stimulation conditions the normal activity of the organism; conversely, when we see how stimulation is the condition of normal physiological activity, as illustrated so admirably in the physiology of respiration as described by Haldane, it need not surprise us that stimulation conditions the development of the nervous system. No static conception of the human body or of any individual organ is in harmony with modern science or modern philosophy.

Thus the genesis and development of the nervous system gives us the point of view and the method for the study of the hygiene of the brain and mind. This is distinctly in harmony with the point of view and method of the newer dynamic physiology and the newer functional psychology.

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